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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/241,347  | 02/02/1999  | HERMANN BUJARD       | BBI-009C4CN         | 8608             |
| 959   | 7590        | 04/20/2004           | EXAMINER            |                  |
| LAHIVE & COCKFIELD, LLP.<br>28 STATE STREET<br>BOSTON, MA 02109 |             |                      | SHUKLA, RAM R       |                  |
|   |             |                      | ART UNIT            | PAPER NUMBER     |
|   |             |                      | 1632                |                  |

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| <b>Office Action Summary</b> | Application No.<br>09/241,347 | Applicant(s)<br>BUJARD ET AL. |
|------------------------------|-------------------------------|-------------------------------|
|                              | Examiner                      | Art Unit                      |
|                              | Ram R. Shukla                 | 1632                          |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 22 September 2003.

2a)  This action is **FINAL**.                            2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

4)  Claim(s) 1,2,4,5,7-11,13-16,18,19 and 21-28 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 1,2,4,5,7-11,13-16,18,19 and 21-28 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)  The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All b)  Some \* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1)  Notice of References Cited (PTO-892)  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3)  Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 8/99.  
4)  Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.  
5)  Notice of Informal Patent Application (PTO-152)  
6)  Other: \_\_\_\_.

**DETAILED ACTION**

1. Applicant's response and amendment filed 9-22-03 have been entered.
2. Amendments to claims 4, 7, 10 and 13 have been entered.
3. Claims 1, 2, 4, 5, 7-11, 13-16, 18, 19 and 21-28 are under consideration.

***Information Disclosure Statement***

The IDS has been considered and signed.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, 4, 5, 7-11, 13-16, 18, 19 and 21-28 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse, whose genome comprises: a first transgene comprising a transcriptional regulatory element functional in cells of the mouse operatively linked to a polynucleotide sequence encoding a fusion protein that inhibits transcription in eukaryotic cells wherein the fusion protein comprises a tet repressor or mutated tet repressor that binds to a tet operator in the absence or presence of tetracycline or tetracycline analog and that is operatively linked to a heterologous polypeptide which inhibits transcription in eukaryotic cells and a second transgene comprising a gene of interest operatively linked to at least one tet operator sequence, wherein said gene of interest confers a detectable and functional phenotype on the mouse when expressed in cells of the mouse, wherein the level of expression of the tet-operator linked gene of interest can be upregulated by administering tetracycline or tetracycline analogue to the mouse and a method for modulating transcription of the second transgene in the transgenic animal by administering tetracycline or

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tetracycline analog to the animal, does not reasonably provide enablement for any other embodiment, for reasons of record set forth in the previous office action of 7-8-99, 9-13-01 and 5-21-03. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

***Response to Arguments***

Applicant's arguments filed 9-23-03 have been fully considered but they are not persuasive. In the page 8 applicants reiterate their invention as recited in claims. Starting with the first full paragraph on page 9, applicants discuss the reference by Wood and argue that scientific process calls for one to make an educated scientific estimation of the expected result which may or may not be correct and that process of making transgenic animals requires screening and the phenotype depends on the gene of interest. Applicants arguments are well taken, however are not persuasive because while an educated estimation can be used, in the case of transgenic animals, the result can not be predicted and as disclosed in the cited arts, one can not predict the relationship between the gene of interest and the phenotype produced. It is noted that phenotype is what is used by an artisan for using the animal. Therefore, if one cannot predict what will be the phenotype, how can an artisan use the transgenic animal. Therefore, the issue is not that one cannot produce a transgenic animal, but the issue is: if it is unpredictable to produce one with a phenotype, how can the animal be used. Applicants argue that they listed several arts in their response of 12-8-99, however these arts were directed to a certain gene of interest and a certain transgenic animal and these arts do not cure the unpredictability. Applicants on page 12 discussed that it was routine in the art to screen litter of group of animals by different methods, however, these arguments again do not cure the unpredictability of the art. While an artisan could screen using the methods describe in the specification or in the arguments or known in the art, one cannot predict what will be the phenotype of an animal.

In summary, applicants' arguments are not sufficient to address all the enablement issues raised in the previous office action and therefore, the scope of the enablement rejection is maintained as discussed above.

***Double Patenting***

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.3218 may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-11 and 13-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent No. 5, 866,755 (2-2-1999), for reasons of record set forth in the previous office action of 7-8-99, 9-13-01 and 5-21-03.

Applicants' request to held the double patenting rejection in abeyance until the indication of allowable claims is acknowledged.

8. Claims 1, 2, 4, 5, 7-11, 13-16, 18, 19 and 21-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record set forth in the previous office action of 5-21-03.

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It is noted that Applicants did not specifically respond to the written description rejection, separately. However, since they discussed the Wood article, it was inferred that they responded to the written description rejection along with the enablement rejection.

9. No claim is allowed.

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

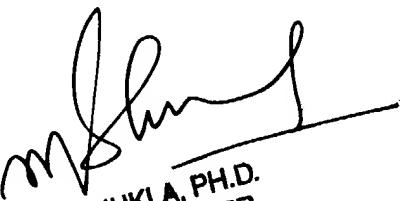
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (571) 272-0735 . The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or

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proceeding should be directed to the William Phillips whose telephone number is (571) 272-0548.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ram R. Shukla, Ph.D.  
Primary Examiner  
Art Unit 1632



RAM R. SHUKLA, PH.D.  
PRIMARY EXAMINER